

REMARKS

To expedite prosecution of preferred embodiments, Applicants have amended the claims. Specifically, claim 1 has been amended to make explicit that which was implicit, namely, that the two nucleic acids do not refer to two molecules of nucleic acids but refer to two populations of nucleic acids that correspond to **at least two genes**. Claims 2, 3 and 10-13 have been amended similarly. Support for this amendment can be found throughout the specification, for example in paragraphs [0031] and [0035]. Support for the amendments can be found throughout the specification and claims 5 and 8, as originally filed. Accordingly, no new matter is introduced by the amendments and their entry is respectfully requested.

The Examiner rejected claims 1-3, and 10-13 35 U.S.C. 103(a) as allegedly being unpatentable over Becker in view of Amexis.

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

The amendments to the claims make explicit that the claims are directed to an analysis of two genes, not two alleles of the same gene. Accordingly, one has, in one reaction at least four different nucleic acid molecule populations, namely, one nucleic acid pair that corresponds to each gene and one standard which corresponds to each gene product but having one base pair difference in them. Neither Becker nor Amexis teach analysis of two separate genes in one reaction using standards for each gene that only differ by one nucleotide. There is nothing in these references that would suggest to a skilled artisan, that the very sensitive method of MALDI-TOF would work in the claimed **quantitative multiplexing assays** (see, pars. 12-14 of the Declaration of Dr. Chun Ming Ding). Indeed, as discussed, the inventors found it surprising that MALDI-TOF system was capable of differentiating such small differences in multiplex reactions and allowing one to **quantitate** the results (see, pars. 14-16 of the Declaration of Dr. Chun Ming Ding).

The Examiner cites an additional reference, Ross et al. ("Ross"), in contending that "multiplexing" reactions for MALDI-TOF analysis were known prior to filing of the present application. However, Ross does **not** teach multiplexing for **quantitative** analysis of at least two genes. Like Amexis, Ross merely measures the allelic variants of the same gene (SNPs) and quantitates only their frequency in pooled nucleic acid sample from different individuals. There

is nothing in Ross that would suggest that one can quantitate the amount of at least two gene products in a single reaction. Certainly, nothing in Ross teaches quantitating at least 5, or 10 or 25 different gene products in one reaction.

In view of the foregoing, Applicants respectfully submit that all claims are in condition for allowance.

Early and favorable action is respectfully requested. Examiner is encouraged to contact the undersigned attorney should there be additional questions regarding the application.

In the event that any additional fees are required, the Commissioner is hereby authorized to charge Nixon Peabody LLP deposit account No. 50-0850.

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Respectfully submitted,

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